Updates on Transplant Surgery

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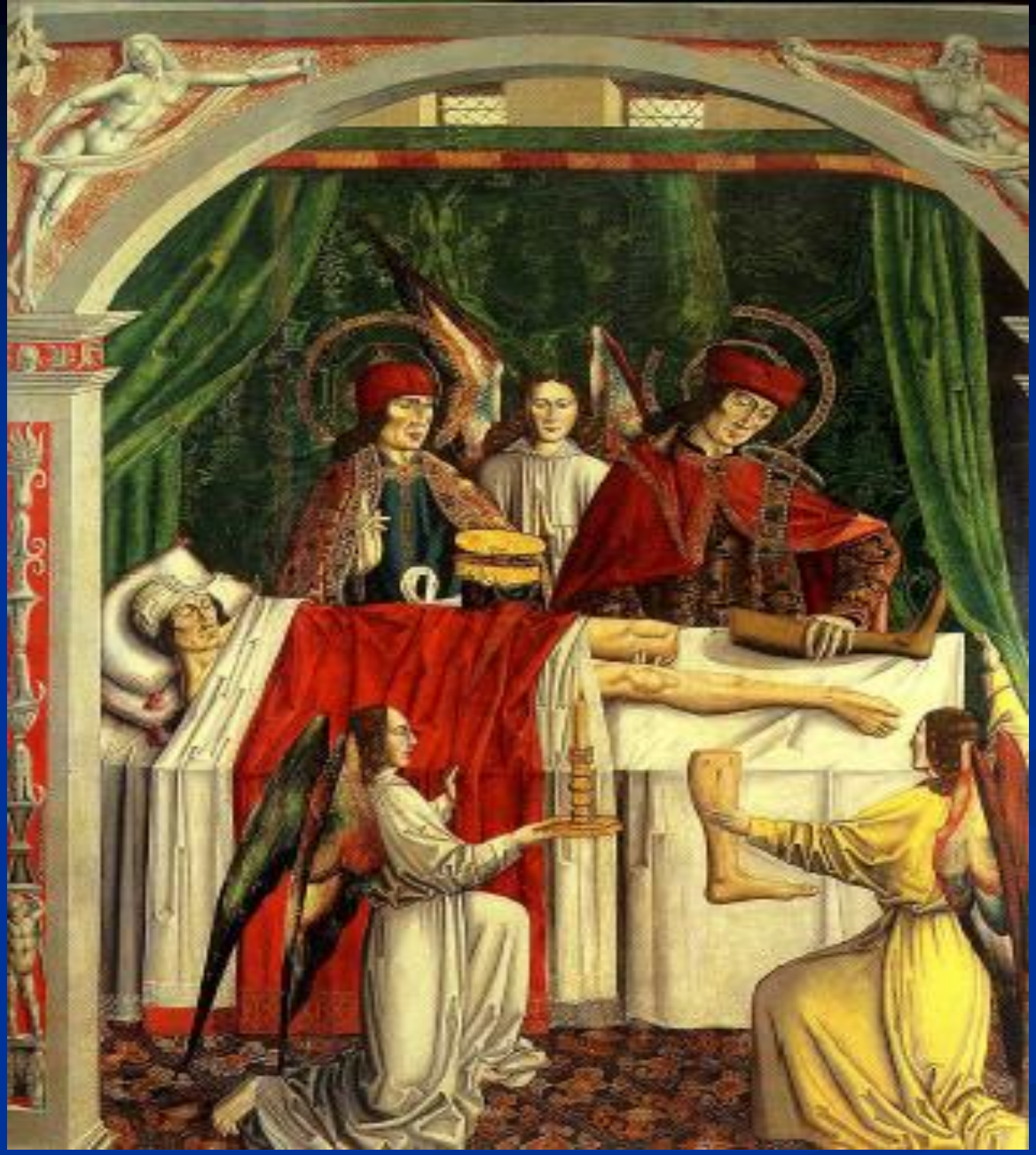
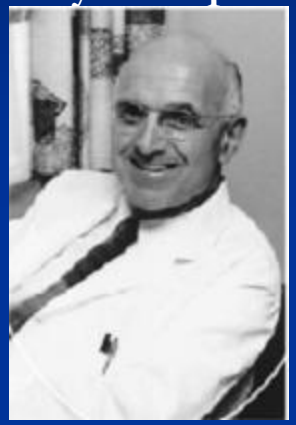


Alonso de Sedano, 1495

U.S. MILESTONS IN TRANSPLANTATION

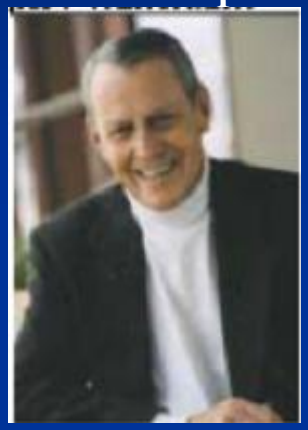
1954

First successful kidney transplant



1967

First successful liver transplant



1981

First successful heart-lung transplant

1983

First successful single lung transplant

1966

First successful pancreas transplant

1968

First successful heart transplant

1983

Cyclosporine, the first of a new group of successful anti-rejection drugs, is approved for commercial use

- Waiting list candidates as of today 5:41pm
- All 108,035
- Kidney 85,460
- Pancreas1,457
- Kidney/Pancreas2,183
- Liver16,101
- Intestine249
- Heart3,139
- Lung1,761
- Heart/Lung79
- Transplants performed January - March 2010
- Total6,712 Deceased Donor5,162
- Living Donor1,550

  - Based on OPTN data as of 06/11/2010

Expansion of Donor Pool

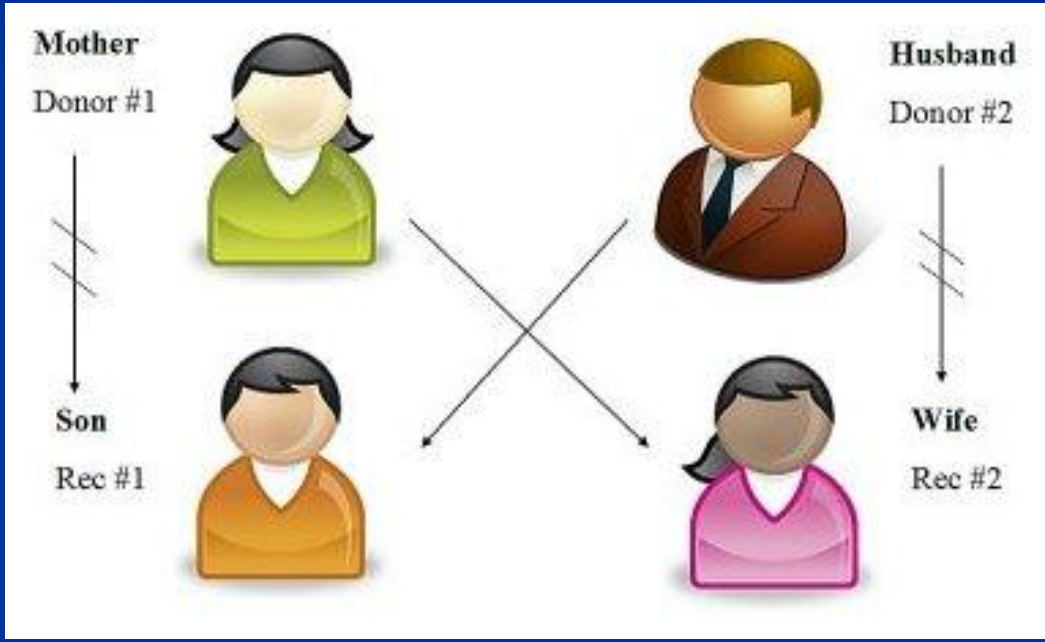
Kidney:

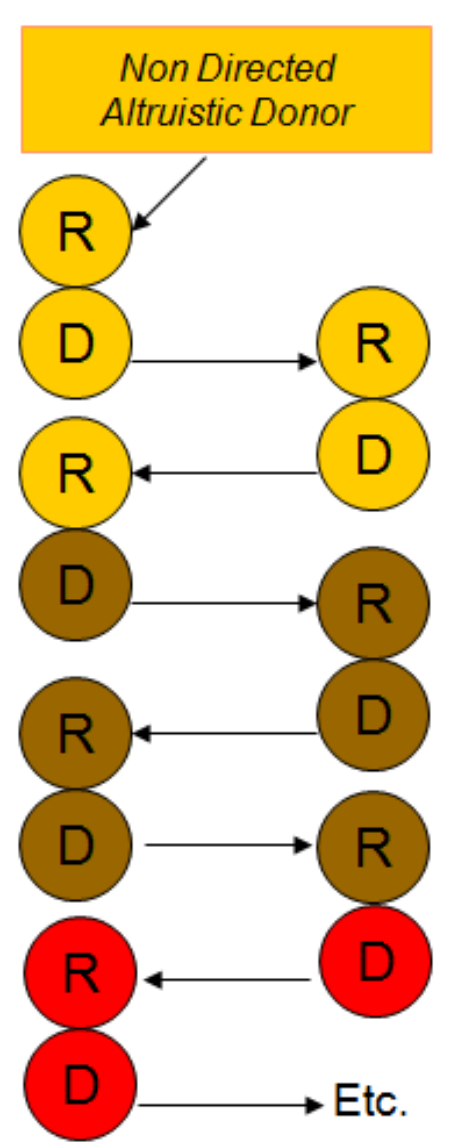
- ECD
- Live donors
- Paired kidney donation
- Desensitization

Liver:

- DCD
- HCV donors
- Live donors

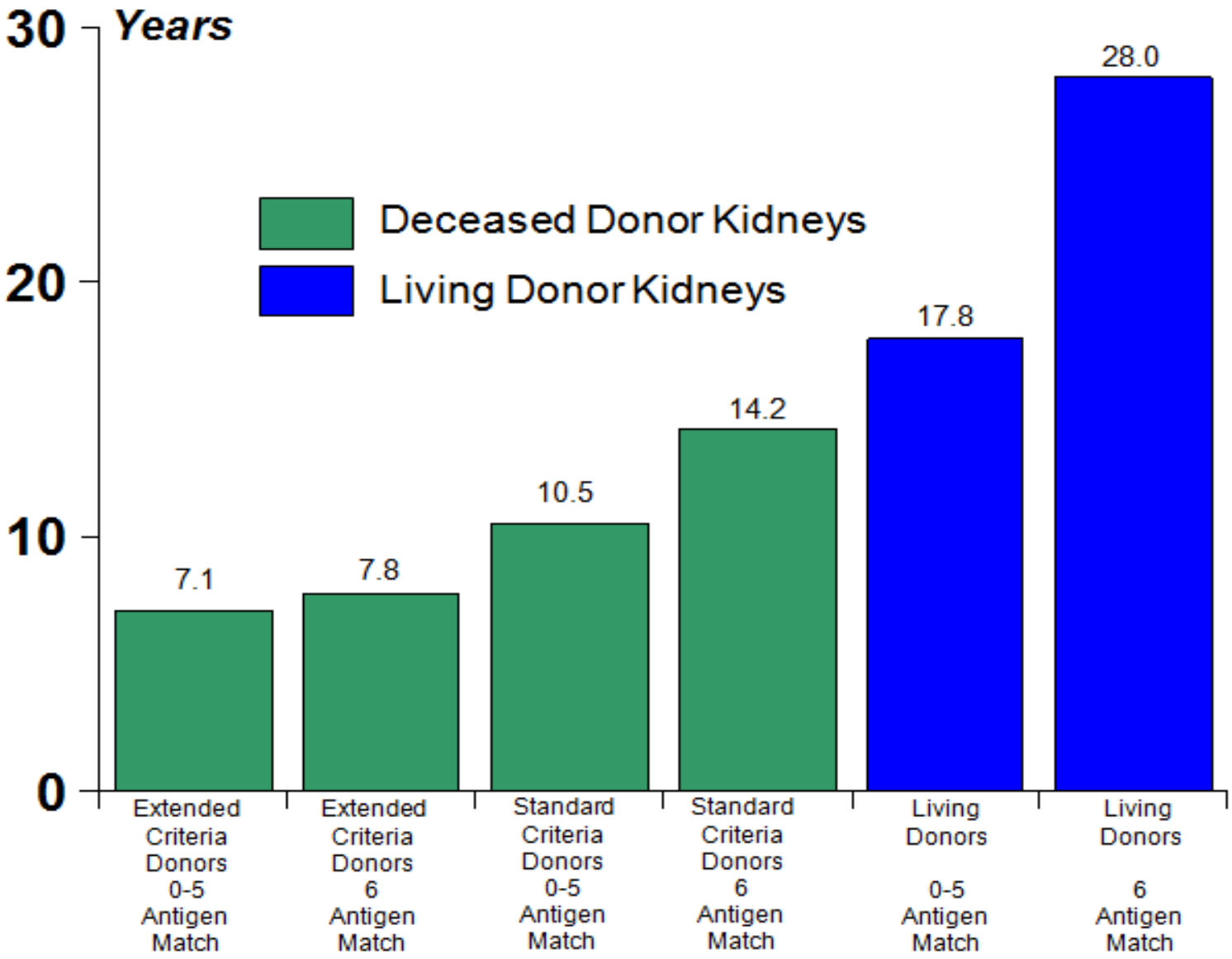
Paired Kidney Donation





Graft Half Life

The Point In Time When Exactly 50% Of The Kidneys Are Still Functioning



Source: Clinical Transplants 2005

Laparoscopic Donor Nephrectomy

- Less hospital stay
- Less post operative pain
- Early return to work.
- Better cosmetic results.

Increased Rates of Donation With Laparoscopic Donor Nephrectomy

Eugene J. Schweitzer, MD,* Jessica Wilson, BSN,* Stephen Jacobs, MD,† Carol H. Machan, BA,‡ Benjamin Philosophe, MD, PhD,* Alan Farney, MD, PhD,* John Colonna, MD,* Bruce E. Jarrell, MD,* and Stephen T. Bartlett, MD*

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Objective

To examine the impact of laparoscopic nephrectomy and recipient education on the proportion of kidney recipients who could identify a potential live donor, and on the live donor (LD) transplantation rate.

Summary Background Data

Laparoscopic donor nephrectomy (LDN) results in less postoperative surgical pain, a shorter hospital stay, and quicker recovery than the standard open donor nephrectomy (ODN). The authors hypothesized that the availability of this less invasive surgical technique would enhance the willingness of family and friends to donate.

Methods

The study population consisted of 3,298 end-stage renal disease patients referred for kidney transplant evaluation between November 1991 and February 2000, divided into three groups. The first group received no formal LD education and had only ODN available. The second group received formal education about the LD process and had only ODN available. The third group had both formal LD education and LDN available. Records were examined to determine what proportion of each group had any potential donors tissue-typed, and the rate at which they received an LD transplant.

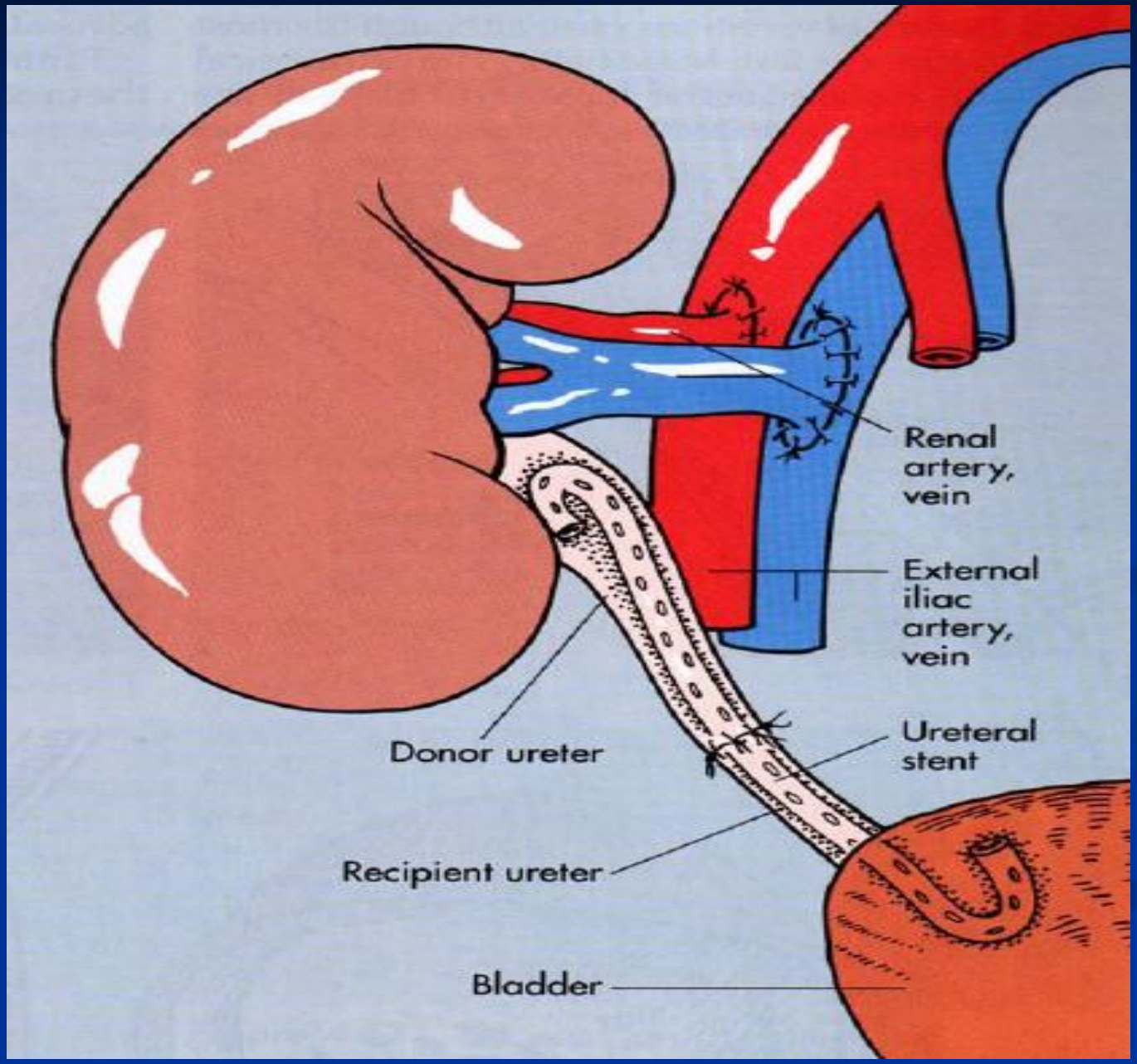
Results

Before LDN availability and formal LD education, only 35.1% of referrals found a potential donor, and only 12.2% received an LD transplant within 3 years. Institution of a formal education program increased the volunteer rate to 39.0%, and 16.5% received an LD transplant. When LDN became available, 50% of patients were able to find at least one potential donor, and within 3 years 24.7% received an LD transplant. Regression analysis indicated that availability of LDN was independently associated with a 1.9 relative risk of receiving an LD transplant. Kaplan-Meier death-censored 1- and 3-year graft survival rates for ODN transplants were 95.8% and 90.6%, versus 97.5% and 94.8% for LDN.

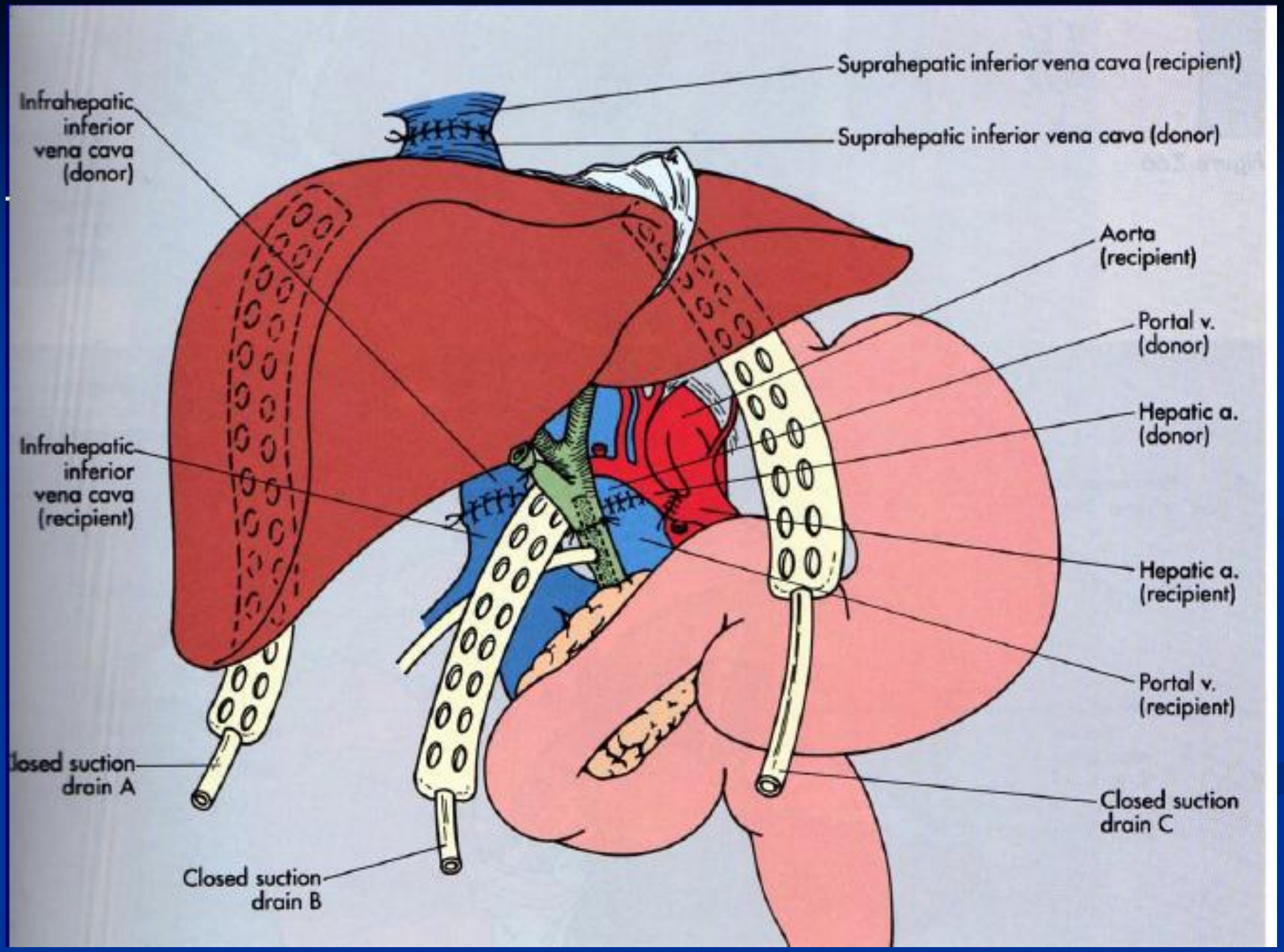
Conclusions

The availability of LDN and an LD family education program has doubled the live donor transplantation rate, and outcomes remain excellent.

3 D Reconstruction of CT angio


Renal
artery,
vein
External
iliac
artery,
vein
Ureteral
stent
Donor ureter
Recipient ureter
Bladder

Laparoscopic Donor Hepatectomy


Suprahepatic inferior vena cava (recipient)
Suprahepatic inferior vena cava (donor)
Infrahepatic inferior vena cava (donor)
Aorta (recipient)
Portal v. (donor)
Hepatic a. (donor)
Infrahepatic inferior vena cava (recipient)
Hepatic a. (recipient)
Portal v. (recipient)
losed suction drain A
Closed suction drain C
Closed suction drain B

Hypothermic Machine Perfusion vs. Cold Storage

Hypothermic Machine Preservation Attenuates Ischemia/Reperfusion Markers after Liver Transplantation: Preliminary Results James V. Guarrera et al , J Surg Res Feb 2010

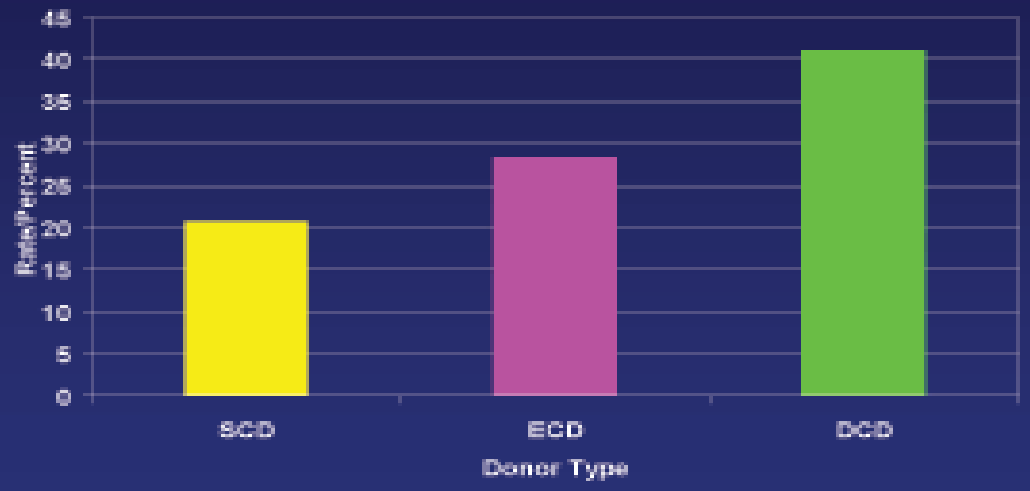
- **Results**

  We saw no differences between HMP and CS in early histologic findings after reperfusion. RT-PCR of reperfusion biopsy samples in the CS group showed high expression of proinflammatory cytokines and ICAM-1. This up-regulation was significantly attenuated by HMP (ICAM-1; $P = 0.0152$) (IL-8; $P = 0.0014$) (TNF-α; $P = 0.0284$). This was confirmed with immunohistochemistry. Albumin was identified in the perfusate throughout HMP.

- **Conclusions**

  HMP significantly reduced proinflammatory cytokine expression compared with CS controls. Further studies of human liver HMP with detailed molecular investigations are now warranted to elucidate benefits of HMP in liver transplantation.

Rate of Delayed Graft Function in Deceased Donor Kidney Transplants Performed January, 2006-October, 2007



OPTN

UNOS

Table 1. Adjusted Logistic Regression for DGF

	Kidney Level	
Transplant Population	OR for pumped vs. not	p-value
All	0.56	less than 0.0001
SCD	0.51	less than 0.0001
DCD	0.76	0.1177
ECD	0.58	less than 0.0001

The Future

- Pulsatile Oxygentated HMP.
- Pulsatile warm perfusion.
- New solutions that can provider better and longer preservation.

Tolerance

Tolerance

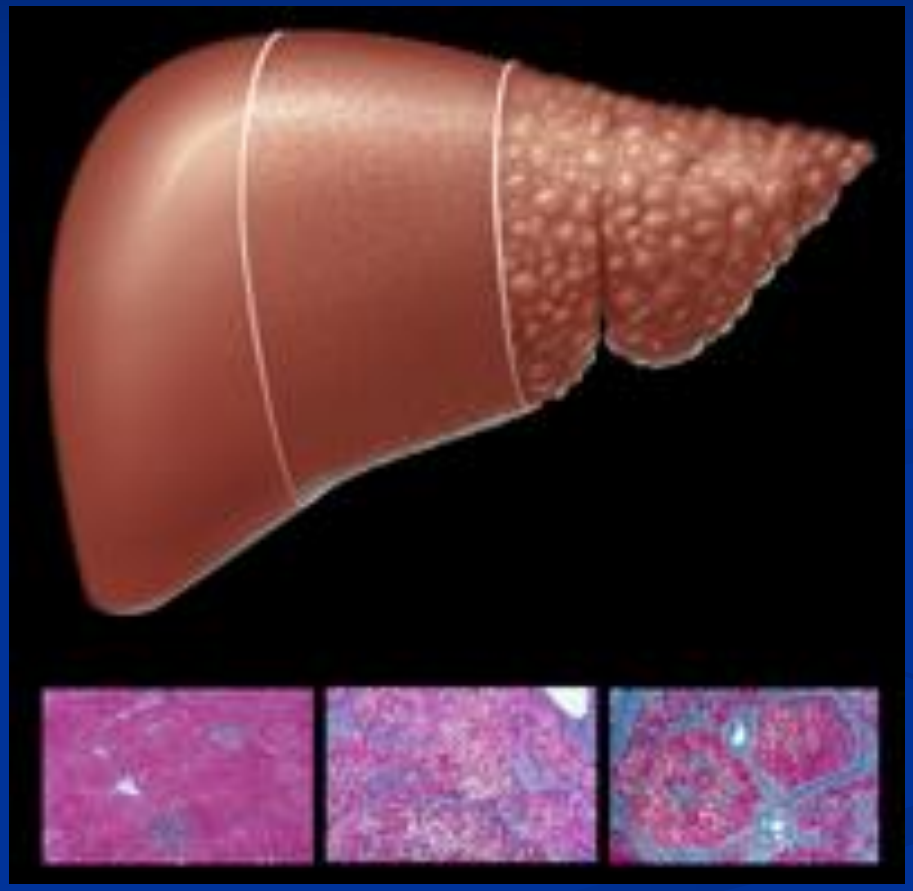
Investigators studied a group of 25 tolerant recipients of renal transplants, of whom 20 had stopped immunosuppressive therapy because of nonadherence. Gene expression in this group was compared with that of 33 renal transplant recipients stable on immunosuppressive drugs and with that of a control group of 42 healthy nontransplanted individuals. Tolerant patients had more numerous B cells in peripheral blood, and genes most predictive of tolerance were B-cell genes.

Induction Therapies

- Interlukin-2 receptor blockers:
- Anti CD-52 monocolonal antibody.
- Antithymocyte antibodies:
  - Thymoglobulin
  - OKT-3

The Good, The Bad & The Ugly

HCC and Liver Transplantation



The Liver, HCV and HCC

An Evolving Story

Global Scope of The Problem

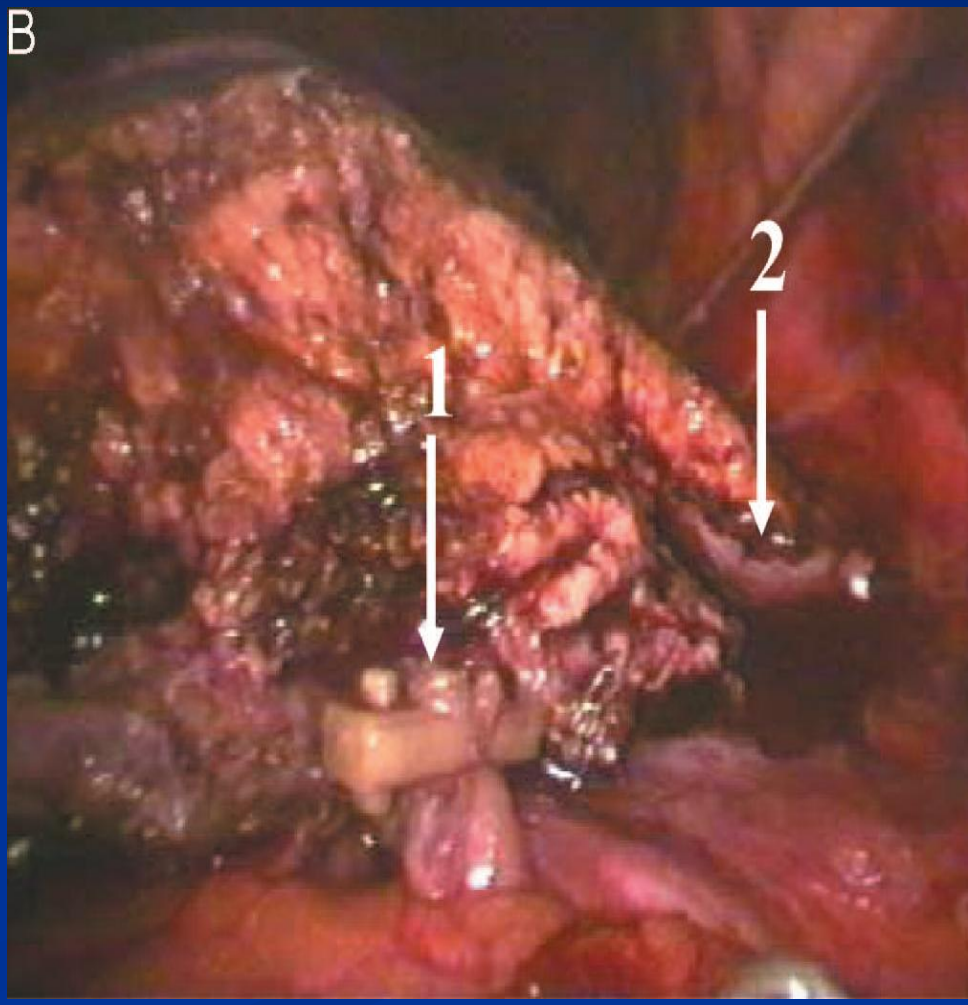
- Highest prevalence in 40-59 year old individuals.
- World wide 550,000 new cases of HCC.
- 5% of human cancers.
- Third leading cause of cancer related deaths.

Surgical Resection

- No extra hepatic disease
- Resectable
  - Non cirrhotic liver
  - Anatomical location
- 1cm safety margin
- Lobectomy, segmentectomy and wegde
- Bench resection and reimplantation.
- Only 10-16% are resectable at the time of presentation.

Oncological priciples

Laparoscopic Hepatectomy



Ablative Therapy

- ~~Ethanol injection.~~
- RFA:
  - Up to 5cm
  - Thermal ablation
  - Tumor viability
- TACE:
- TAY-90
- Irreversible Electroporation (Nano knife).

Liver Transplantation

- What is death?
- Can we extend life?
- Whose life do we extend?
- At what price the extension of life?
- Just because we can extend life should we?

There are always *three* patients to consider—the patient, the donor, and the person on the waiting list who likely died because the organ went to your patient.

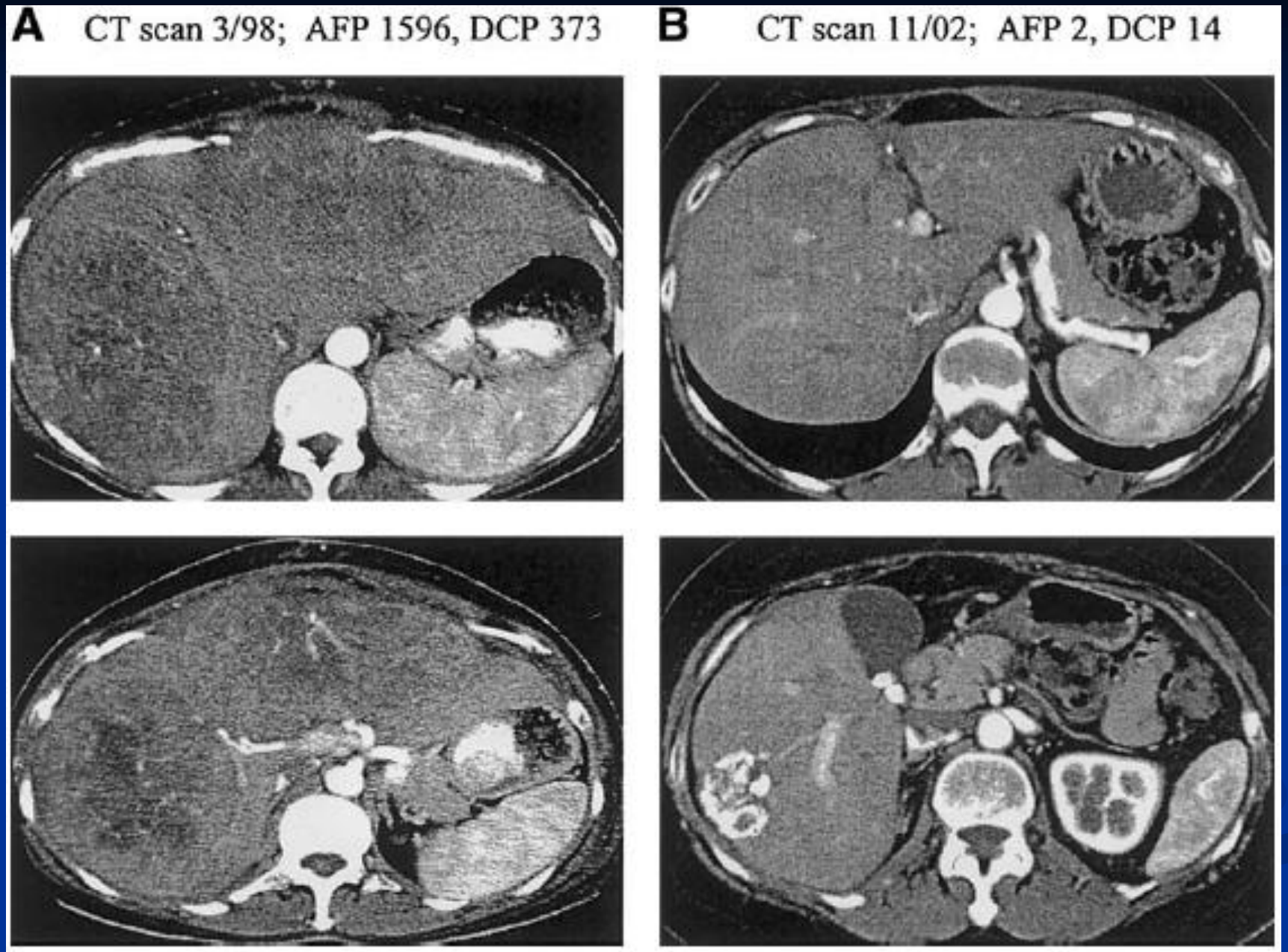
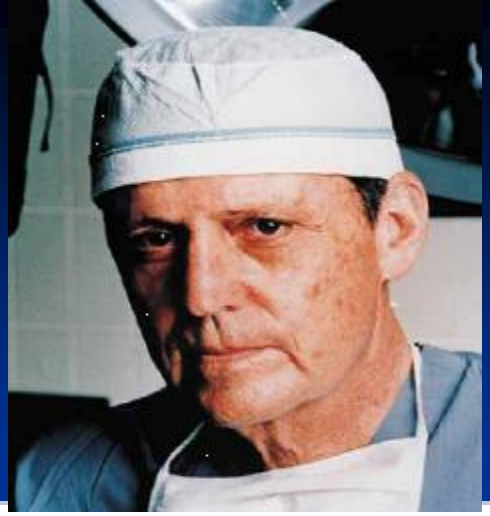


Figure 1. (A) CT scan March 1998; AFP 1596, DCP 373. (B) CT scan November 2002; AFP 2, DCP 14.

A dilemma remains in regard to the best treatment course to pursue at this time. We have debated the following options:

1. Liver transplantation
2. Hepatic resection
3. Further TACE
4. Observation



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ORTHOTOPIC LIVER TRANSPLANTATION IN NINETY-THREE PATIENTS

T. E. Starzl, M.D., F.A.C.S., K. A. Porter, M.D., C. W. Putnam, M.D., G. P. J. Schroter, M.D., C. G. Halgrimson, M.D., F.A.C.S., R. Weil III, M.D., F.A.C.S., M. Hoelscher, M.D., and H. A. S. Reid, M.R.C.(PATH.)

From the Departments of Surgery, the University of Colorado Medical Center and the Veterans Administration Hospital, Denver; and the Department of Pathology, St. Mary's Hospital and Medical School, London

Liver graft survival

Recipient's Age	1 year %	5 year %
< 1 Year	81.1	63.5
1-5 Years	77.8	67.0
6-10 Years	84.4	75.3
11-17 Years	87.4	67.O
18-34 Years	80.7	64.2
35-49 Years	83.0	65.6
50-64 Years	82.1	65.3
65 +	78.8	59.2

Selection Criteria

- **Milan Criteria**

  Single tumor ≤ 5cm or

  3 ≤ tumors each ≤ 3 cm.

- **UCSF criteria**

  Single tumor ≤ 6.5 cm or 2-3 tuors ≤ 4.5cm with total tumor diameter

  ≤ 8cm

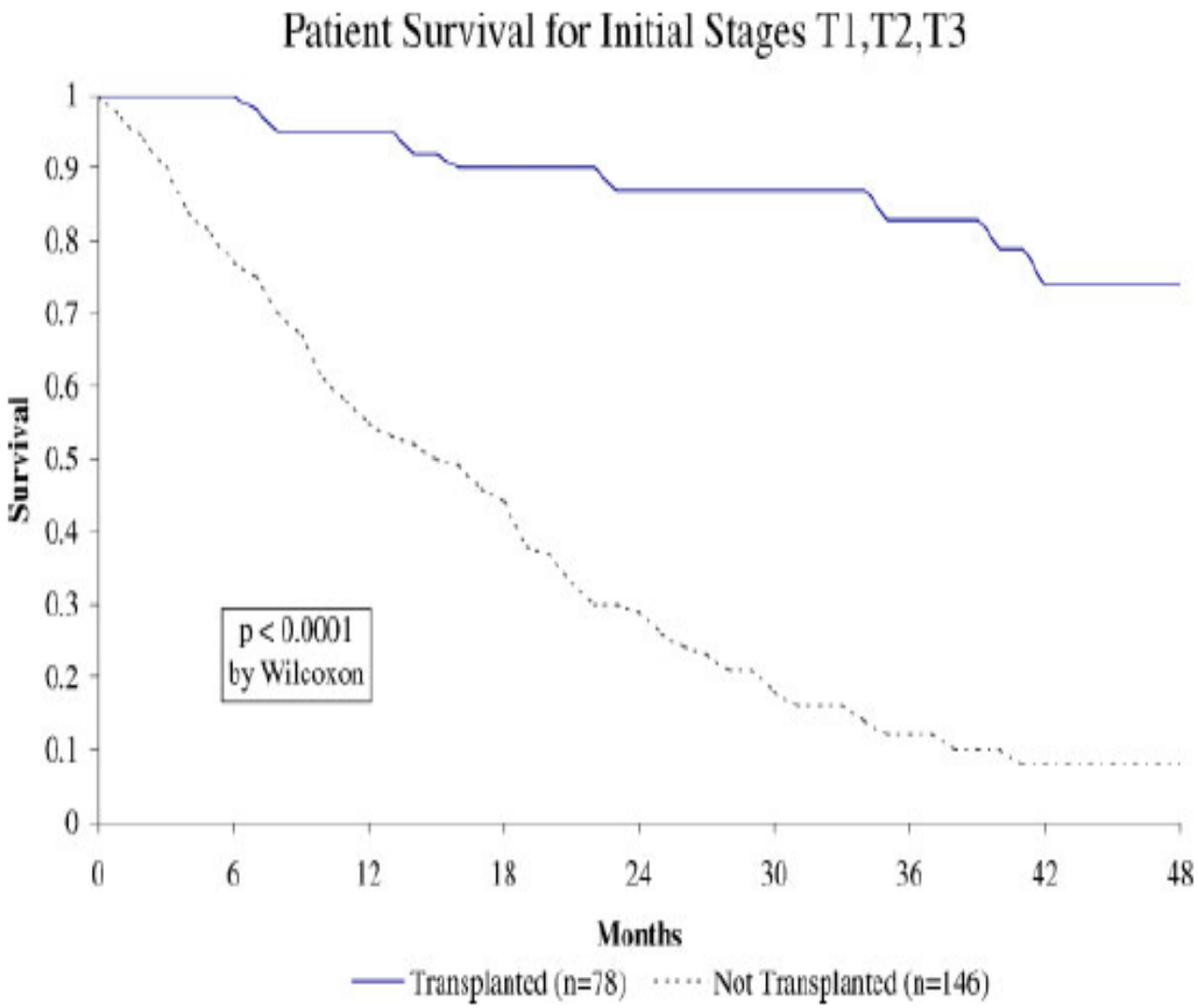


Fig. 3. Patient survival for initial stages T_1, T_2, T_3 (transplanted vs. not transplanted).

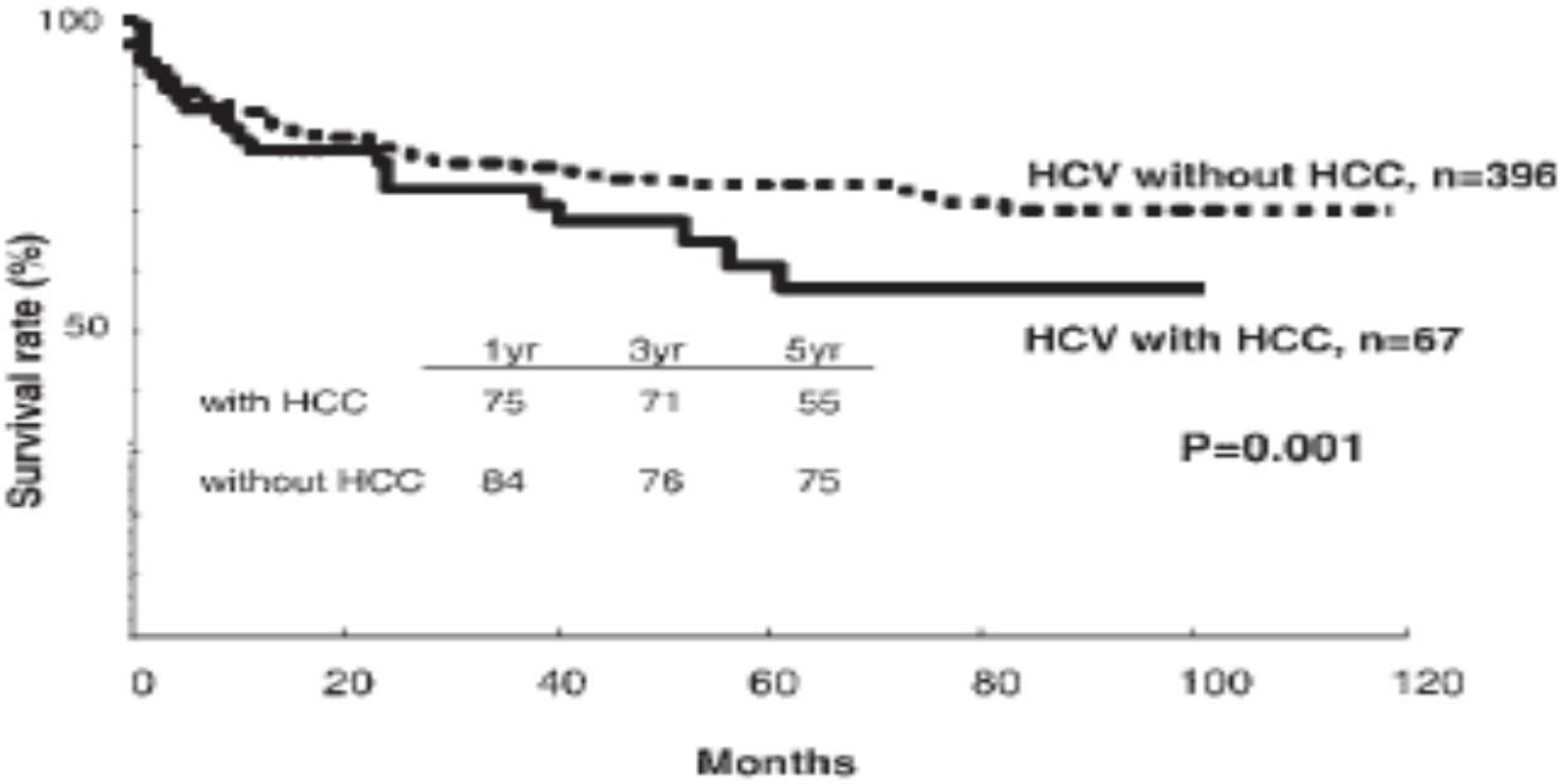


Figure 1. Kaplan-Meier Patient Survival Curves. Overall patient survival following HCV with HCC compared to a cohort of patients who had received OLT for HCV without HCC.

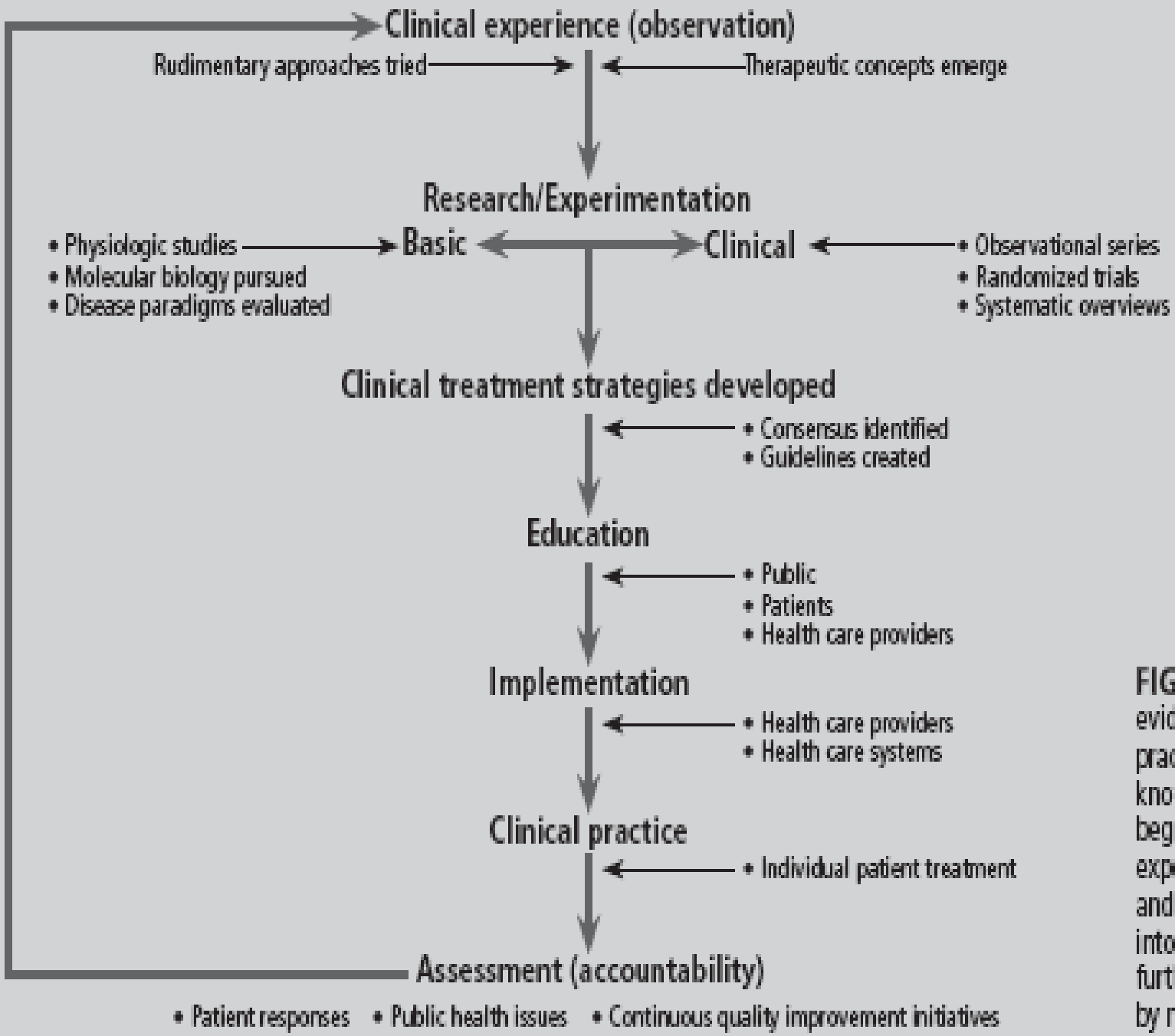


FIGURE 1. Flow chart of evidence-based medical practice. The drive for new knowledge is circuitous, beginning with clinical experience and observation and ultimately feeding back into clinical practice and further research prompted by new experience.

Stem cells are unspecialized cells that have two important characteristics that distinguish them from other cells in the body.

First, they can replenish their numbers for long periods through cell division.

Second, after receiving certain chemical signals, they can differentiate, or transform into specialized cells with specific functions, such as a heart cell or nerve cell.

Sources of Stem Cells

- Embryonic stem cells (ESCs)

  are derived from 4- to 5-day-old embryos. At this stage, the embryos are spherical and are known as blastocysts. Each blastocyst consists of 50 to 150 cells and includes three structures: an outer layer of cells, a fluid-filled cavity, and a group of about 30 pluripotent cells at one end of the cavity. This latter group of cells, called the inner cell mass, form all the cells of the body.

- Adult stem cells

  are undifferentiated cells that are found in small numbers in most adult tissues. However, they are also found in children and can be extracted from umbilical cord blood. A more accurate phrase is "somatic stem cells," although this phrase has yet to be generally adopted. The primary roles of adult stem cells in the body are to maintain and repair

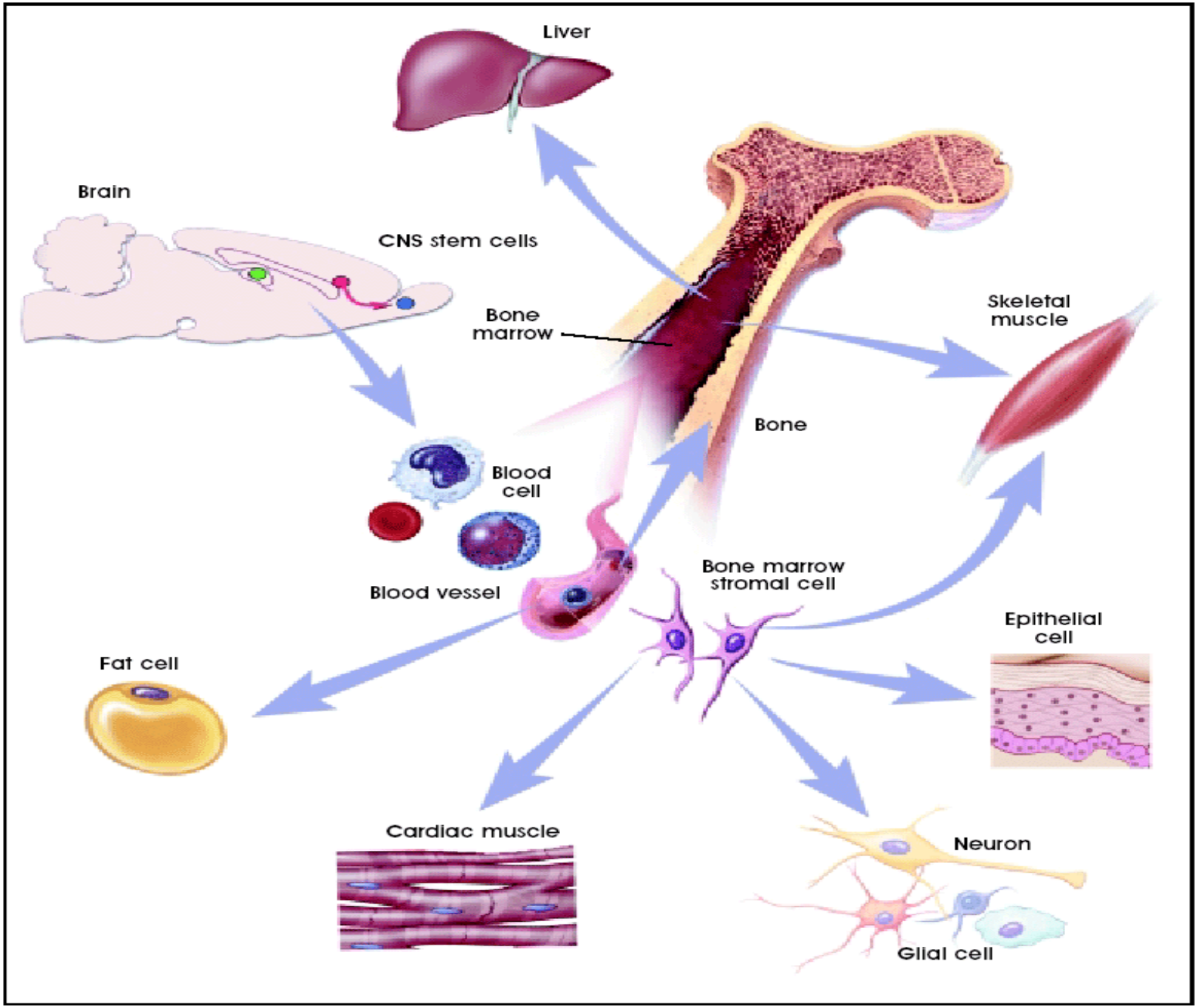


Figure 4.2. Preliminary Evidence of Plasticity Among Nonhuman Adult Stem Cells.

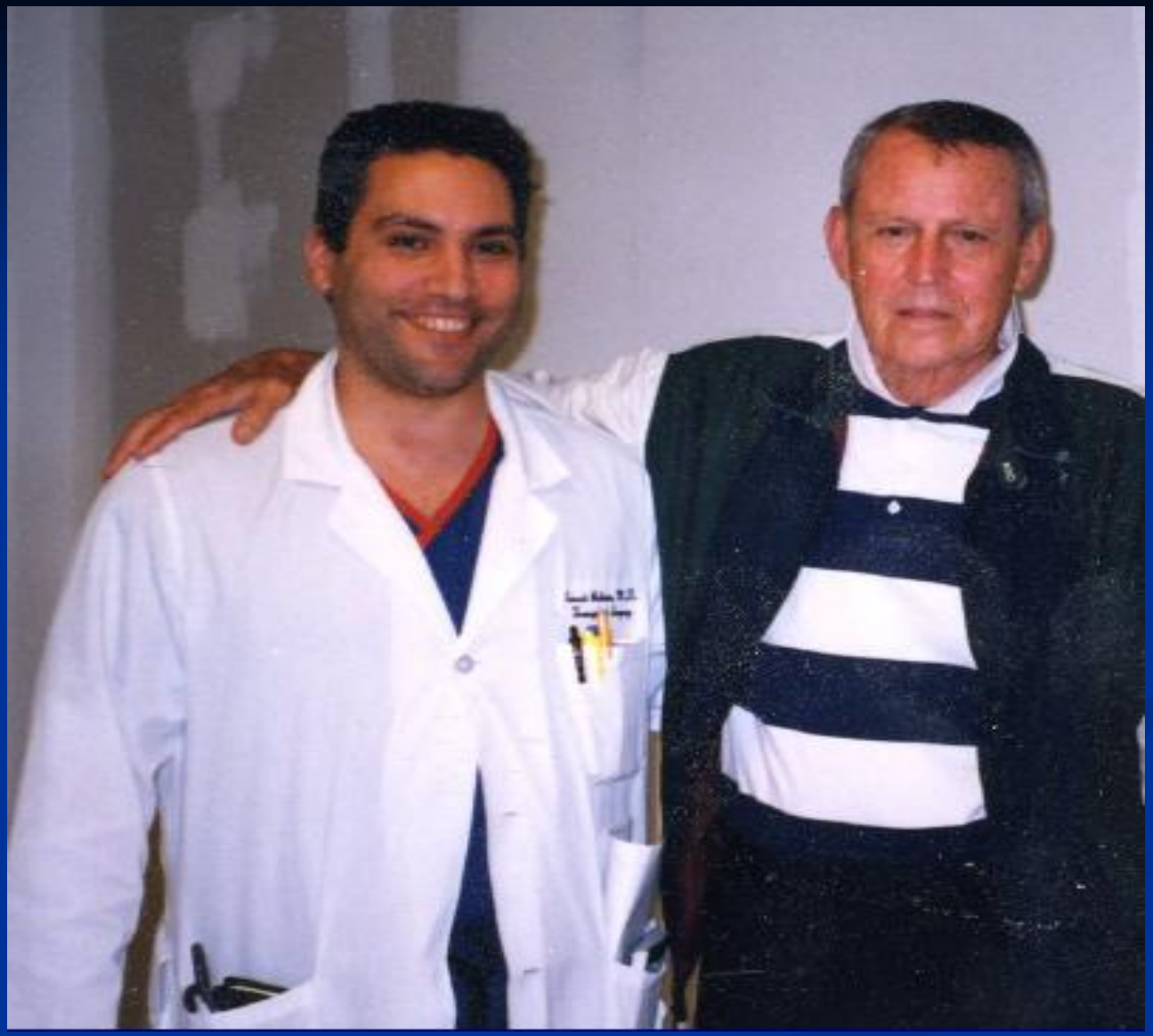
Cell Prolif. 2008 Feb;41 Suppl 1:115-25.

Long-term clinical results of autologous infusion of mobilized adult bone marrow derived CD34+ cells in patients with chronic liver disease. Habib NA, et al, Imperial College, London.

- Between 1 x 10(6) and 2 x 10(8) CD34(+) cells were isolated and injected into the portal vein or hepatic artery. The patients were monitored and followed up for 12-18 months.
- Four patients showed an initial improvement in serum bilirubin level, which was maintained for up to 6 months. There was marginal increase in serum bilirubin in three of the patients at 12 months, while the fourth patient's serum bilirubin increased only at 18 months post-infusion.
- Computed tomography scan and serum alpha-foetoprotein monitoring showed absence of focal lesions.
- The study indicated that the stem cell product used was safe in the short and over long term, by absence of tumour formation. The investigation also illustrated that the beneficial effect seemed to last for around 12 months. This trial shows that stem cell therapy may have potential as a possible future therapeutic protocol in liver regeneration.

Ethics of Transplantation

- A practitioner should act in the est intrest of the patient (Salus aegroti suprema lex)
- "First, do no harm" (primum non nocere), from the Hippocratic Oath
- Autonomy is a patient's right to choose or refuse treatment (Voluntas aegroti suprema lex)
- Justice – concerns the distribution of scarce health resources, and the decision of who gets what treatment
- Dignity – the patient (and the person treating the patient) have the right to dignity
- Truthfulness – patients shoud not be lied to, and deserves to know the whole truth about their illness and treatment



Thank you